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Surgery in the treatment of nonseminomatous testicular tumors

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CHAPTER VIII

SUMMARY

The role of surgery in the treatment of patients with a nonseminomatous testicular tumor (NSTT) is described in this thesis on the basis of five articles. The study was started at the end of 1977 when the chemotherapeutic cisplatin became available at the Groningen University Hospital.

The introduction (Chapter I) discusses two distinct groups of germ cell tumors of the testis: seminomatous and nonseminomatous tumors. All patients discussed in this thesis were treated for a NSTT. The histological classification of testicular tumors is briefly discussed, using the nomenclature of the World Health Organization. It is also pointed out that some subgroups of testicular tumors produce specific tumor markers demonstrable in the patient's serum. The clinical staging of NSTT is also outlined, with special reference to the Peckham staging now in use and that of Skinner and Scardino which was used in the past. Surgery can be of great importance both in the diagnosis and in the treatment of testicular tumors. Surgery is diagnostic if the tumor size is determined in an exploratory operation, in which tissue may also be removed for histologic examination. Surgery is therapeutic if it comprises tumor resection.

A fairly detailed account is presented of the past and current methods of treating these patients.

Finally, four questions are formulated which prompted this study. The answers to these questions are discussed in the subsequent five chapters.

Chapter II discusses 54 patients with NSTT in clinical Stage I, followed in an expectant strategy during the period 1982-1985. This expectant strategy or wait-and-see policy means that, if no metastases are demonstrated after hemiorchiectomy, patients are merely submitted to very frequent check-ups during subsequent years. This wait-and-see policy has the advantage over the policy focused on retroperitoneal lymph node dissection (RLND), as accepted up to 1982, that some 80% of the patients can be saved an operation which carries a degree of morbidity, the important complication being retrograde ejaculation disorders. Since diagnostic radiology was initially considered not sufficiently reliable in screening for retroperitoneal metastases, an exploratory laparotomy was performed to complete the dissemination study in 1982 and 1983. Once it was found that this intervention supplied virtually no additional information, it was performed *only if strictly indicated from 1984 on*.

The recurrence rate with a wait-and-see policy is about twice as high as that with RLND (20% versus 10%), but these recurrences respond very well to combination chemotherapy with cisplatin. In order to reduce recurrences an attempt was

made to identify possible predictive criteria. However, neither the histology of the testicular tumor nor the serum tumor marker levels were found to be of prognostic value in this study.

It is concluded that a wait-and-see policy is reliable as long as patients are submitted to frequent check-ups. If this cannot be ensured, then RLND remains indicated.

Chapter III discusses 25 patients in whom retroperitoneal lymph node metastases of a NSTT were treated with combination chemotherapy comprising cisplatin, vinblastine and bleomycin (PVB) between 1978 and April 1983. In 21 cases this chemotherapy was preceded by an exploratory laparotomy for definitive tumor staging. During chemotherapy one patient died from digestive tract hemorrhage resulting from a very large tumor invading the intestinal wall and the aorta. In the remaining 24 cases the serum tumor marker levels normalized after chemotherapy. All these patients underwent a laparotomy at which residual tumor tissue (if any) was removed.

Four patients proved to have no demonstrable residual tumor. Of the remaining 20 patients, 13 showed necrosis and fibrosis in the residual tumor while 7 had a mature teratoma. Malignant tumor tissue was no longer found.

At the end of the study these 24 patients were all still alive after an average follow-up of 56 months. Two had developed a recurrence for which one patient was still being treated at completion of this study. The other proved to have developed a secondary malignancy in a teratoma remnant after 73 months.

On the basis of a comparison of the histology of the primary tumor with that of the residual tumor, and in view of the fact that radiological findings on the retroperitoneum are not entirely reliable, it is advisable to make the indication for laparotomy following chemotherapy at least partly dependent on the histology of the primary tumor, i.e. the presence of a teratoma component.

Chapter IV discusses 53 patients likewise given PVB chemotherapy during the period 1978-1983. These patients had lymphogenous metastases below and above the diaphragm (Stage III) and/or lung metastases (Stage IV). After the remission-induction chemotherapy 41 showed normalization of the serum tumor marker levels. They were further evaluated and, in the end, exploratory surgery was performed in 35 patients. Malignant tumor tissue was found in the residual tumor in 4 patients, mature teratoma in 16, necrosis and fibrosis in 14 patients, while one patient no longer had any lesions. At completion of the study 38 patients (72%) were still alive after an average follow-up of 65 months. Six patients (10%) had developed a recurrence, which led to a fatal outcome in two. The therapeutic results are further discussed on the basis of the histology of the residual tumor and the initial tumor volume.

It is concluded that the prognosis is poor when the serum tumor marker levels are still increased after remission-induction chemotherapy. This is in contrast to the

situation of patients in whom the presence of malignant tumor is demonstrable only from the histology of the resected residual tumor. This study clearly showed that the indication for laparotomy and/or thoracotomy following chemotherapy should be made partly dependent on the presence of a teratoma component in the primary tumor. Finally, the initial tumor volume was found to be of unmistakable prognostic significance.

Chapter V discusses the growing mature teratoma with reference to three case histories, selected from 86 patients treated during the period 1978-1983 by PVB chemotherapy in view of a NSTT with metastases.

A growing mature teratoma can be suspected on clinical grounds when in the course of the follow-up a recurrence is observed in patients with a teratoma component in the primary tumor with normal serum tumor marker levels. Such a recurrence always dictates surgical exploration because, in addition to a growing mature teratoma, malignant tumor tissue or secondary malignancy may be involved. En bloc resection of the recurrent tumor is sufficient in the treatment of a growing mature teratoma.

In the discussion it is pointed out that tumors of this type are histologically benign but cytogenetically malignant. Other studies have shown that remnants of mature teratoma tissue can develop in the course of time to large, usually cystic tumors. For patients with a teratoma component in the primary tumor this implies the necessity of trying, after chemotherapy, to resect all residual tumor tissue in order to prevent subsequent development of a growing mature teratoma.

Chapter VI describes the investigations required for reliable determination of the condition of the retroperitoneal lymph nodes in patients with a NSTT. This is done with reference to 32 cases in which the assessments of the abdominal CT scan and lymphography were compared with the findings at exploratory laparotomy. The comparison showed that the absence of metastases can be reliably demonstrated with the CT scan, while lymphography and laparotomy provide but little additional information. The presence of metastases can likewise be reliably demonstrated with the CT scan. Attempts to determine the tumor stage and tumor volume on the basis of these data, however, are less reliable. Lymphography supplies hardly any additional information in this respect, but exploratory laparotomy does give much additional information. It is concluded that the CT scan is sufficient to delineate clinical Stage I. For exact delineation of higher stages an additional exploratory laparotomy is required. According to this study there is no longer an indication for lymphography to search for retroperitoneal lymph node metastases in patients with a NSTT.

In the general discussion the current strategy is evaluated on the basis of the results reported in this thesis. Desirable changes in strategy are outlined in view of this evaluation. These changes in strategy concern the diagnosis as well as the treatment of nonseminomatous testicular tumors.